OPEN ACCESS

Clinical science

Predisposing factors, clinical and microbiological insights of bacterial keratitis: analysis of 354 cases from a leading French academic centre

Clara Bertret,[1] Juliette Knoeri ,[1] Loic Leveziel,[1] Tristan Bourcier,[2] Françoise Brignole-Baudouin,[1] Lilia Merabet,[1] Nacim Bouheraoua,[1] Vincent Michel Borderie [1]

[1]Hôpital National des 15-20, Paris, France
[2]Ophthalmology, UDS, Strasbourg, France

Correspondence to
Professor Vincent Michel Borderie, Hôpital National des 15-20, Paris 75571, France; vincent.borderie@upmc.fr

Received 25 January 2024
Accepted 9 May 2024

Check for updates

© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Bertret C, Knoeri J, Leveziel L, *et al*. *Br J Ophthalmol* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjo-2024-325261

ABSTRACT

Aims To report an epidemiological update of bacterial keratitis (BK) in a tertiary ophthalmology centre over 20 months compared with a previous study on the same timeframe from 1998 to 1999.

Methods 354 patients with BK documented by microbiological corneal scraping or resolutive under antibiotics treatment from January 2020 to September 2021 were analysed retrospectively.

Results One or several risk factors were found in 95.2% of patients: contact lens wear (45.2%), ocular surface disease (25.0%), systemic disease (21.8%), ocular trauma (11.9%) and ocular surgery (8.8%). The positivity rate of corneal scrapings was 82.5%, with 18.2% polybacterial. One hundred seventy-five (59.9%) bacteria were Gram-negative, and 117 (40.1%) were Gram-positive. The most common bacteria were *Pseudomonas aeruginosa* (32.5%), *Moraxella* spp (18.1%) and *Staphylococcus aureus* (8.2%). Final visual acuity (logarithm of the minimum angle of resolution) was associated with age (r=+0.48; p=0.0001), infiltrate size (r=+0.32; p<0.0001), ocular surface disease (r=+0.13; p=0.03), ocular trauma (r=-0.14; p=0.02) and contact lens wear (r=−0.26; p<0.0001). Gram-negative bacteria were responsible for deeper (r=+0.18; p=0.004) and more extensive infiltrates (r=+0.18; p=0.004) in younger patients (r=−0.19; p=0.003). Compared with the previous period, the positivity rate of corneal scrapings and the proportion of Gram-negative bacteria, especially *Moraxella* spp, increased. All *P. aeruginosa* and *Moraxella* spp were sensitive to quinolones, and all *S. aureus* were sensitive to both quinolones and methicillin.

Conclusion Contact lens wear remained the leading risk factor. The bacteria distribution was reversed, with a predominance of Gram-negative bacteria and increased *Moraxella* spp.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Wearing contact lenses is the leading risk factor for bacterial keratitis.

WHAT THIS STUDY ADDS

⇒ We report an inversion of the Gram-positive-Gram-negative balance with increased *Moraxella* spp over 20 years and an increase in the positivity rate of corneal scrapings.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The rate of antibiotic resistance is very low with protocols using three broad-spectrum antibiotics to treat severe bacterial keratitis.
⇒ Implementation of a strict protocol for corneal scraping results in a high positivity rate of microbiological tests.

INTRODUCTION

Infectious keratitis represents a significant cause of corneal opacification, potentially leading to vision loss.[1] Visual prognosis depends on a quick diagnosis and appropriate antimicrobial therapy. The most common germs are bacteria in many countries such as Brazil (78.9%),[2] Canada (86%),[3] the UK (92.8%),[4] Australia (93.1%),[5] except China (52.7%)[6] and India (35.7%).[7] The main symptoms are acute ocular pain, photophobia, redness and decreased vision. Bacterial keratitis (BK) rarely occurs without predisposing factors such as trauma, contact lens (CL) wear, ocular surface disease (OSD), systemic immunosuppression or ocular surgery.[8] The most commonly isolated bacteria are Gram-positive, mainly coagulase-negative *Staphylococci* belonging to the ocular surface commensal flora.[1] However, some studies have identified *Pseudomonas aeruginosa* as the leading bacterium due to climatic and geographical variations.[4 5 9 10] Intensive broad-spectrum topical antibiotics are first used to treat severe BK, followed by an adaptation to the identified pathogen or the clinical response.[11] Management of BK is currently challenged by the emergence of antimicrobial resistance (AMR), particularly in the USA and Asia.[12–14] Epidemiological studies in Europe report the rate of AMR in BK, but no data are available in France.[4 10]

An epidemiological BK study was conducted in our tertiary centre between 1998 and 1999.[15] The present study aimed to compare two large series of patients suffering from BK with a 20-year gap to identify potential changes in BK risk factors, clinical presentations, prognosis and microbiological epidemiology. The secondary objective was to evaluate the sensitivity of bacteria to antibiotics.

Br J Ophthalmol: first published as 10.1136/bjo-2024-325261 on 26 June 2024. Downloaded from http://bjo.bmj.com/ on August 10, 2024 by guest. Protected by copyright.

Table 1 Population characteristics at baseline and clinical outcomes (n=354) compared with the previous study 1998–1999 (n=291)

Parameters	Period 2020–2021 (n=354)	Period 1998–1999 (n=291)	P value
Populations characteristics			
Sex ratio (male/female)	1.03	1.09	0.99
Age (years)	51±21	39±18	0.008
Right eye/left eye	0.97	0.84	0.37
Hospitalisation time (days)	6.0 (0–41)	9.0 (3-60)	<0.0001
Initial visual acuity (logMAR)	1.64±0.82	0.79±1.0	<0.0001
Referred to the emergency unit	168 (47%)	72 (24%)	<0.0001
First symptoms-to-first examination time (days)	4.4±6.4	NA	
Risk factors			
Contact lens wear	160 (45%)	151 (50%)	0.25
Ocular surface disease	88 (25%)	64 (21%)	0.39
Systemic disease	77 (22%)	51 (17%)	0.13
Ocular trauma	42 (12%)	45 (15%)	0.24
Ocular surgery	31 (9%)	12 (4%)	0.004
No risk factors	17 (5%)	28 (9%)	0.02
Infiltrate characteristics			<0.0001
Area (mm^2)			
<5	158 (45%)	123 (42%)	
5–15	104 (29%)	115 (38%)	
>15	92 (26%)	62 (20%)	
Depth			<0.0001
<1/3	129 (36%)	232 (77%)	
1/3–2/3	147 (42%)	39 (13%)	
>2/3	78 (22%)	29 (10%)	
Anterior chamber inflammation			
Tyndall	223 (63%)	73 (24.4%)	<0.0001
1+	66 (19.0%)	NA	
2+	81 (23.0%)	NA	
3+	44 (12.0%)	NA	
4+	32 (9.0%)	NA	
Hypopion	118 (33%)	18 (6%)	<0.0001
Neovascularisation	54 (15%)	35 (12%)	0.03
Perforation	18 (5%)	NA	
Prior treatment			
Topical antibiotics	125 (35%)	72 (24%)	0.002
Topical steroids	19 (5.4%)	9 (3.1%)	0.16
Positive microbiological identification	292 (82%)	204 (68%)	<0.0001
Treatment			
Mean treatment time	49.0±44.9 days	NA	
Surgical treatment			
Amniotic membrane transplantation	78 (22%)	NA	
Therapeutic penetrating keratoplasty	13 (4%)	2 (0.6%)	0.01
Evisceration	3 (0.8%)	2 (0.6%)	0.79
Outcomes			
Mean follow-up time (days)	117.9±165.3	90	
Final visual acuity (logMAR)	0.82±0.94	NA	

Shown are the number (percentage) and mean (±SD).
NA, not available.

MATERIAL AND METHODS

Study design

The study period ranged from January 2020 to September 2021. All patients hospitalised in the French National Vision Hospital (Hôpital National des 15-20, Paris, France) infectious ocular disease unit for BK, defined as a corneal stromal infiltrate with an epithelial defect documented by microbiological corneal scraping or resolutive under antibiotics treatment, were included. Only the most affected eye was included for bilateral BK. A total of 354 BK in 354 eyes were included. Nine BK were bilateral. Hospitalisation for infectious keratitis was decided if the patient presented severity criteria on examination in the emergency or consultation units. The severity criteria were the same as those already described in 1998–1999[11]: location of the infiltrate within the 3 mm of the visual axis, infiltrate size >2 mm, anterior chamber inflammation, worsening under 24-hour antibiotic treatment, corneal transplantation, single eye patient, immunosuppressed patient, bilateral keratitis. Diagnosis and management of BK were performed according to written standard operative procedures.

Microbiological analysis

An ophthalmologist performed corneal scrapings at the earliest stage using a sampling kit including different tools, that is, a sterile scalpel blade 15T and an e-Swab (Copan Diagnostics, Murrieta, California, USA). Samples from e-Swab were inoculated under sterile conditions on various solid and liquid media that facilitate the growth of bacteria, including chocolate agar (PVX), 5% sheep blood agar, Schaedler broth and a Sabouraud medium. Specimens from the scalpel blade were smeared on two slides and stained with May Grünwald Giemsa (MGG). The bacterial cultures were incubated in 5% CO_2 at 35±2°C and examined daily for growth for at least 7 and 15 days. The culture was considered positive when a bacterium was identified on at least one of three media. The isolated bacteria were identified by biochemical galleries, and the susceptibility to antibiotics was evaluated by the diffusion disc method and interpreted according to the guidelines established by the French Society of Microbiology and the European Committee on Antimicrobial Susceptibility Testing. Bacterial multiplex PCR was performed in cases of suspected BK with negative direct examination and culture. Fungal, *Acanthamoeba* and viral co-infections were systematically and simultaneously investigated.

Corneal imaging

In some cases with atypical clinical features or history, in vivo confocal microscopy was performed to rule out *Acanthamoeba* and filamentous fungal keratitis.

Data collection

The following data were collected: age, sex, duration of the symptoms before consultation, antibiotics or other treatments before consultation, initial and final visual acuity (logarithm of the minimum angle of resolution (logMAR)), causative bacteria and its susceptibility to antibiotics, ocular complications and surgical management. Infiltrate size (<5 mm^2, 5–15 mm^2, >15 mm^2), infiltrate location (peripheral, central), infiltrate depth (<1/3, 1/–-2/3, >2/3 of the total corneal thickness), anterior chamber inflammation (Tyndall scored from 1+ to 4+, hypopyon) were assessed by slit-lamp examination. The following risk factors were evaluated: corneal trauma, CL wear (soft, rigid, scleral), OSD (bullous keratopathy, recurrent keratitis, peripheral ulcerative keratitis, endothelial decompensation, exposure keratitis, palpebral malposition, neurotrophic keratitis, dry eye syndrome), systemic diseases (diabetes, chronic alcoholism, systemic immunosuppression, psychiatric illness) and prior ocular surgery.

BK medical management

All hospitalised BK-suspect patients received three fortified topical antibiotics (ie, piperacillin (20 mg/mL), gentamicin

Br J Ophthalmol: first published as 10.1136/bjo-2024-325261 on 26 June 2024. Downloaded from http://bjo.bmj.com/ on August 10, 2024 by guest. Protected by copyright.

Table 2 Population characteristics by main risk factors

Risk factors	Number of cases	Aetiologies	Age (years)	First symptom-to-first examination time (days)	Final visual acuity (logMAR)	Most frequent bacteria
Contact lens wear	160 (45.2%)	150 soft lenses 8 rigid lenses 2 scleral lenses	38±15	3.6±5.9	0.37±0.54	*Pseudomonas aeruginosa* (n=80; 50.0%) Coagulase-negative staphylococci (n=16; 10.0%) *Serratia* spp (n=10; 6.2%)
Ocular surface disease	88 (25.0%)	36 neurotrophic keratitis 21 eyelid malposition 19 exposure keratitis 14 endothelial dysfunctions 8 bullous keratitis 5 recurrent keratitis 3 herpetic keratitis 3 peripheral ulcerative keratitis	70±18	5.3±6.4	1.53±1.04	*Moraxella* spp (n=27; 30.7%) *Staphylococcus aureus* (n=9; 10.2%) *Streptococcus pneumoniae* (n=8; 9.1%)
Systemic disease	77 (21.8%)	33 diabetes 18 immunosuppressive diseases 13 psychiatric illness 10 chronic alcoholism	64±18	5.1±5	1.16±1.01	*Moraxella* spp (n=25; 32.5%) *P. aeruginosa* (n=9; 11.7%) Coagulase-negative staphylococci (n=9; 11.7%)
Ocular trauma	42 (11.9%)	32 cases with a foreign body 10 acute corneal trauma	52±19	3.3±3	0.65±0.83	*Moraxella* spp (n=8; 19.0%) Coagulase-negative staphylococci (n=5; 11.9%) *S. aureus* (n=4; 9.5%)
Ocular surgery	31 (8.8%)	19 penetrating keratoplasties 7 refractive surgeries 2 DMEKs 1 intracorneal ring segment 1 retinal surgery 1 eyelid surgery	55±21	7.2±13	1.15±0.92	*P. aeruginosa* (n=6; 19.3%) *S. aureus* (n=5; 16.1%) *S. pneumoniae* (n=5; 16.1%)

Shown are the numbers (percentage) and mean (±SD). DMEK: Descemet Membrane Endothelial Keratoplasty

(15 mg/mL) and vancomycin (50 mg/mL)), administrated hourly for 48 hours, and followed by one drop every 2 hours until improvement. This association of three fortified antibiotics is commonly used in France or Europe.[16] Piperacillin or ticarcillin is used for its action against most Gram-positive and Gram-negative bacteria. Vancomycin is used as a second antibiotic to act against *methicillin-resistant Staphylococcus* and *Streptococcus pneumoniae* with reduced sensitivity to penicillin. Gentamicin is used as a third antibiotic for its rapid bactericidal action in synergy with piperacillin and vancomycin. Topical dual antibiotic therapy was adapted according to the clinical response, germ and antibiogram as soon as the microbiological results were available. The therapeutic protocol was not modified except for replacing ticarcillin with piperacillin compared with the period of 1998–1999.[15]

Statistical analysis

Statistical analysis was performed using MedCalc software Ltd V.19 (8400 Ostend, Belgium). Descriptive data were reported in mean and SD. LogMAR visual acuity was used to calculate mean and SD. Analysis of variance, χ^2 test, Wilcoxon rank-sum test and Mann-Whitney U test assessed relationships between initial BK characteristics, care protocol and outcomes. The relationships between final visual acuity, risk factors and BK initial clinical characteristics were evaluated with multiple linear regression.

RESULTS

Table 1 summarises population characteristics at baseline and clinical outcomes. CL wear was the most common risk factor found in 160 BK (45.2%) (table 2). A previous BK history was observed in 28 BK (7.9%) and associated with the presence of systemic disease (p=0.002). Females were predominant in the CL wear group (62.5%; p<0.0001) as opposed to the trauma group with 76.2% males (p=0.0005). The rate of microbiological identification was 82.5% (292/354). Two hundred nineteen germs (61.9%) were identified by direct examination, 258 (72.9%) by culture and 9 (2.5%) by PCR multiplex. 9.6% (34/354) of the corneal samples were identified on direct examination with no further growth in culture, 15.8% (56/354) were grown on only one of the three media (33 coagulase-negative staphylococci (CoNS), 20 *Propionibacterium acnes*, 3 *Corynebacterium* spp) and 57.0% (202/354) on at least two of the culture media. Prior antibiotics did not modify the microbiological positivity rate (84.0% vs 77.1%; p=0.12). Gram-negative bacteria (n=175; 59.9%) were predominant compared with Gram-positive bacteria (n=117; 40.1%) (table 3). The most frequent bacteria were *P. aeruginosa* (95; 32.5%). No *Staphylococcus aureus* resistant to methicillin was noted, even in recurrent BK (table 4). Gram-negative bacteria featured a higher Tyndall effect than other germs (p<0.0001). *Moraxella* BK featured larger and deeper infiltrates than other bacteria (p<0.0001) and was more frequently associated with chronic alcoholism (p=0.002). Among the most frequent germs, mean visual acuity (logMAR) was in ascending order: *S. pneumoniae* (1.59±1.06), *Moraxella* spp (1.30±1.02), *P. aeruginosa* (0.70±0.81), *S. aureus* (0.60±0.62), CoNS (0.48±0.74), *P. acnes* (0.27±0.59). Corneal scrapings were polybacterial in 53/292 (18.2%) cases. The predominant bacteria in polybacterial culture were *Moraxella* spp (19/53; 35.8%) only associated with Gram-positive bacteria (7 *Staphylococcus coagulase-negative*, 5 *S. aureus*, 5 *P. acnes*, 2 *Corynebacterium* spp). These polyBK were more frequently associated with systemic disease (p=0.048), CL wear (p=0.038), older patients (59.2±22.6 years vs 50.0±21.0; p=0.004), and worse final visual acuity (1.18±1.01 vs 0.75±0.92; p=0.006) compared with monobacterial keratitis.

Br J Ophthalmol: first published as 10.1136/bjo-2024-325261 on 26 June 2024. Downloaded from http://bjo.bmj.com/ on August 10, 2024 by guest. Protected by copyright.

Table 3 Bacteria identified in patients with bacterial keratitis

Bacteria	N	%
Gram-negative bacteria	175	59.9
Gram-negative bacilli		
Pseudomonas aeruginosa	95	32.5
Moraxella spp	53	18.1
Moraxella nonliquefaciens	19	6.5
Moraxella lacunata	16	5.5
Serratia marcescens	13	4.4
Pseudomonas stutzeri	1	0.3
Klebsiella oxytoca	1	0.3
Klebsiella pneumoniae	3	1.0
Citrobacter koseri	2	0.7
Escherichia coli	1	0.3
Haemophilus influenzae	1	0.3
Others	5	1.7
Gram-positive bacteria	117	40.1
Gram-positive cocci	87	29.8
Staphylococcus aureus	24	8.2
Streptococcus pneumoniae	20	6.8
Coagulase-negative staphylococci	20	6.8
Staphylococcus lugdunensis	1	0.3
Streptococcus sanguinis	2	0.7
Streptococcus parasanguinis	2	0.7
Streptococcus mitis oralis	2	0.7
Streptococcus dysgalactiae spp	1	0.3
Gram-positive bacilli	30	10.3
Propionibacterium acnes	23	7.9
Corynebacterium spp	7	1.7

Amniotic membrane transplantation (AMT) was performed for delayed epithelial healing in 78 BK (22.0%). The most common BK requiring AMT was *S. pneumoniae* keratitis (40.0%), followed by *Moraxella* (34.0%), *P. aeruginosa* (27.0%) and *S. aureus* (16.7%) keratitis. BK requiring AMT featured poorer initial and final visual acuity (p<0.001). Corneal perforation occurred in 18 BK (5.1%). The average age of patients with perforated BK was higher (67.8 vs 50.5 years; p=0.0001). Thirteen therapeutic penetrating keratoplasties (3.7%) and three eviscerations (0.8%) were performed (table 5).

In multivariate analysis, poorer final logMAR visual acuity was associated with age (r=0.48; p=0.0001), infiltrate size (r=0.32; p<0.0001), OSD (r=0.13; p=0.03). CL wear (r=−0.26; p<0.0001), ocular trauma (r=-0.14; p=0.02) and absence of risk factor (r=−0.14; p=0.02) were associated with better final visual acuity. Gram-negative bacteria were responsible for deeper (r=0.18; p=0.004) and more extensive infiltrates (r=0.18; p=0.004) in younger patients (r=−0.19; p=0.003) compared with Gram-positive bacteria.

A comparison with the previous study is presented in table 1. Gram-negative bacteria were predominant (59.9% vs 17.0%) as opposed to Gram-positive bacteria (40.1% vs 83.0%), with an increase in *Moraxella* spp (18.1% vs 0.3%). *P. aeruginosa* was more frequent among CL wearers (50.0% vs 12.0%). The main risk factor remained CL wear, followed by OSD. All patients received fortified antibiotic eye drops vs 213 (71%) in the previous study. Compared with the 1998–1999 BK series, the 2020–2021 BK series featured deeper infiltrates with more anterior segment inflammation, more frequent corneal vascularisation, poorer initial visual acuity, a higher microbiological identification rate, shorter hospitalisation time and required more therapeutic keratoplasties.

DISCUSSION

Changes in BK risk factors, microbiological agents and clinical presentation could be shown over 20 years. An increase in the prevalence of *Moraxella* spp was noted in our series as in the UK.[17 18] *Moraxella* spp are associated with systemic diseases, particularly diabetes, chronic alcoholism and OSDs.[17 19 20] Chronic alcoholism was also a risk factor for *Moraxella* keratitis in our study. As in the Zafar study, 42.3% of the *Moraxella* keratitis patients had a hypopyon.[19] The infiltrates were deeper and needed more AMT for delayed epithelial healing. AMT improves the healing process and reduces corneal haze and neovascularisation. It is associated with better visual recovery and less corneal vascularisation at 6 months than topical treatment alone.[21] A high number of AMTs (22.0%) were performed in our population to accelerate healing and prevent corneal perforation.

CL wear remained the leading risk factor for BK, with 160 cases (45.2%).[8 22] The incidence of BK secondary to CL wear ranges from 0.33% in the West Bengal area[23] to 50.3% in France.[15] In the CL group, patients were younger, consulted quickly, had a better visual prognosis and had more Gram-negative BK, especially *P. aeruginosa*, compared with the other groups. The study's high rate of CL wearers may explain the high rate of *P. aeruginosa*. CL wear induces hypoxia and hypercapnia of the cornea, making these eyes more susceptible to infection. Mechanisms of biofilm formation, epithelial disruption and alteration of the antimicrobial quality of the tear film also favour the development of BK.[24]

Numerous studies report polymicrobial keratitis with widely varying rates, from 2.4%[25] to 23.9%.[5] In the study by Lim *et al*,[26] the rate of identified polybacterial keratitis was 3.0% with two Gram-negative bacteria as the most frequent combination, and in the study by Ting *et al*, 10.7% with *Streptococcus* spp and coagulase-negative *Staphylococci* combination. As in Jones's study, polybacterial keratitis, particularly *Moraxella* spp, was associated with organisms commonly isolated from normal conjunctival flora.[27] The real pathogenic impact of these associated commensal germs can be questioned.

Table 4 Antibiotic susceptibility rates of the main bacteria isolated

	Piperacillin	Ceftazidime	Amikacin	Gentamicin	Erythromycin	Ciprofloxacin	Levofloxacin	Rifamycin	Vancomycin
Staphylococcus aureus (n=24)	16.7% (4/24)	100%	100%	100%	70.8% (17/24)	100%	100%	100%	100%
Streptococcus pneumoniae (n=20)	NT	NT	100%	100%	85.0% (17/20)	100%	100%	100%	100%
Pseudomonas aeruginosa (n=95)	98.9% (94/95)	98.9% (94/95)	100%	98.9% (94/95)	NT	100%	NT	NT	NT
Moraxella spp (n=53)	NT	100%	100%	100%	100%	100%	100%	100%	NT

NT, none tested.

Br J Ophthalmol: first published as 10.1136/bjo-2024-325261 on 26 June 2024. Downloaded from http://bjo.bmj.com/ on August 10, 2024 by guest. Protected by copyright.

Table 5 Demographic, risk factors, clinical and microbiological characteristics of 16 bacterial keratitis requiring emergency surgery

Sex, age	Risk factors	Previous topical treatment	Microbiological identification	Cause of surgery	Hospitalisation time (days)	Final visual acuity (logMAR)
Therapeutic penetrating keratoplasty						
M, 69	Neurotrophic keratitis	–	*Moraxella nonliquefaciens*	Impending perforation	14	LP
F, 78	Diabetes, chemotherapy	DXM	*Moraxella* spp, *Corynebacterium* spp	Perforation	4	NLP
M, 75	Palpebral malposition in Lyell's syndrome	–	*Streptococcus pneumoniae*, CoNS	Perforation	6	NLP
F, 27	Intracorneal rings (D3)	–	*S. pneumoniae*	Impending perforation	12	0.40
M, 65	Diabetes	–	*M. nonliquefaciens*	Perforation	5	NLP
M, 24	Penetrating keratoplasty (Y14)	DXM, tobramycin	*Pseudomonas aeruginosa*	Graft dehiscence	5	0.20
F, 77	Soft contact lens	Azithromycin	*P. aeruginosa*	Perforation	13	LP
M, 45	Penetrating keratoplasty (Y2), interferon	DXM, ciclosporin	*Pseudomonas stutzeri*	Impending perforation	36	2
M, 45	Graves' exophthalmos, steroids	–	*M. nonliquefaciens*	Perforation	13	2.30
M, 84	Palpebral malposition with trichiasis, diabetes	Picloxydine	*S. pneumoniae*, *Klebsiella pneumoniae*	Perforation	34	LP
F, 79	Penetrating keratoplasty (Y5, Y2)	–	CoNS	Perforation	17	LP
M, 57	Ocular trauma	Fortified antibiotic	–	Perforation	13	2
M, 78	Neurotrophic keratitis, cognitive disorders	–	CoNS, *Corynebacterium striatum*	Perforation	18	LP
Evisceration						
M, 35	Vernal keratoconjunctivitis, LASIK (Y15)		*Moraxella lacunata*	Phthisis	14	NLP
M, 85	Ocular trauma, hemopathy		*S. pneumoniae*	Endophthalmitis, cellulitis	9	NLP
F, 55	Diabetes		*Streptococcus dysgalactiae* spp	Endophthalmitis, cellulitis	14	NLP

CoNS, coagulase-negative staphylococci; D, day; DXM, dexamethasone; F, female; LP, light perception; M, male; NLP, no light perception; Y, year.

The 82% microbiological positivity rate was significantly higher compared with the previous period (68%)[15] and recent series (49.3% in China[9] and 64.3% in Saudi Arabia[28]). The inoculation protocol was modified between 1998 and 1999 and 2020 and 2021. Previously, all culture media were inoculated by the ophthalmologist with a dry swab in the examination room, whereas in the present study period, they were inoculated under sterile conditions by the microbiologist using e-Swab in the laboratory. Thanks to its enhanced capillary action and hydraulic liquid absorption, e-Swab enables several culture media to be inoculated with a single sample.[29] There is no significant difference in microbiological results between direct and indirect inoculation by e-Swab of culture media, except for direct examination with Gram stain. To correct this, in our protocol, specimens from the scalpel blade were smeared directly on two slides after the corneal scraping with e-Swab.[30] A second solid culture medium of blood agar type was added to interpret contamination. This change in the inoculation procedure and replacing the dry swab with an e-Swab allowed greater control of culture media storage conditions and limited external contamination of culture media.

Older age and larger infiltrate size were known risk factors for poor visual prognosis, as in the Portsmouth corneal ulcer study,[31] Nottingham's study[32] and the study by Miedziak *et al*.[33] OSD was also associated in our series with a poor visual prognosis, particularly the delay between the first symptoms and the emergency department assessment. Conversely, CL wear, ocular trauma and the absence of risk factors were protective prognostic factors.

AMR to common broad-spectrum antibiotics was low compared with studies in the USA[13] or Asia.[6 14] This finding may not apply to BK after keratoplasty. We recently reported that bacterial resistance is common in those patients, and it may be associated with prolonged use of preventive topical antibiotics that result in the selection of resistant bacteria.[30]

The most commonly identified resistant species in the literature were *P. aeruginosa* and *Staphylococcus* spp for moxifloxacin and *S. aureus* for methicillin (MRSA).[14 34 35] We found only three resistant *P. aeruginosa* (one to piperacillin, one to ceftazidime and one to gentamicin), and no MRSA over the period 2020–2021, similar to the very low MRSA rate of 0.07%–1% in the UK.[4 17] All *Moraxella* spp were sensitive, as in the study by Termote *et al* in Vancouver.[36] The systematic use of three fortified topical antibiotics (ie, piperacillin (20 mg/mL), gentamicin (15 mg/mL) and vancomycin (50 mg/mL)) for severe keratitis and the frequent use of topical quinolones in combination with another antibiotic could explain this low rate. Patients with recurrent BK (7.9%) had no further AMR in our study.

There is no international consensus on the treatment of BK. Despite the risk of increasing bacterial resistance, fourth-generation quinolones such as moxifloxacin are now widely used as monotherapy in South America, Africa and Oceania.[16] A randomised comparative study between fourth-generation fluoroquinolones and fortified antibiotics in the treatment of BK showed no differences.[37] However, the resistance rate to quinolones is high in India[38] and increases in the USA.[35] In our study, all severe BK were treated initially with three topical fortified antibiotics, followed by a dual antibiotic therapy adapted to the antibiogram according to the clinical course.

Our present study features some limitations. This monocentric retrospective series aimed to describe BK in patients requiring hospitalisation. The inclusion of BK referred to a tertiary care centre led to a selection bias towards the most severe cases. In contrast to the 1998–1999 study[15] and the literature,[2 9 17 18 31] Gram-negative bacteria were the most frequent contaminants. The included BK cases were more severe than 20 years ago. The predominance of Gram-negative bacteria may explain this severity.[24] Besides, Ung *et al* reminds us that without standardised criteria for laboratory identification, the worldwide microbiological results should be interpreted with caution because most

Br J Ophthalmol: first published as 10.1136/bjo-2024-325261 on 26 June 2024. Downloaded from http://bjo.bmj.com/ on August 10, 2024 by guest. Protected by copyright.

commensal organisms of the eyelids and ocular surface are Gram-positive and more likely to contaminate media.[1 24 36]

CONCLUSION

P. aeruginosa, favoured by CL wear, was the principal causative agent of severe BK. An increase in *Moraxella* spp was noted over 20 years. Teaching patients about CL hygiene should remain a priority for practitioners.

Contributors Conceptualisation: JK, LL and VMB. Data curation: CB, JK, LL and LM. Formal analysis: JK, CB, LL and VMB. Funding acquisition: VMB. Investigation: JK, CB and LL. Methodology: JK, LM, VMB, NB and TB. Project administration: JK and VMB. Guarantor: VMB Supervision: VMB, JK and LL. Validation: JK, LL, VMB, LM, NB, FB-B and TB. Writing—original draft: CB, JK, LL and LM. Writing—review and editing: CB, JK, LL, LM, VMB, NB, FB-B and TB.

Funding This work was supported by Sorbonne Université, Paris, France.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The Ethics Committee of the French Society of Ophthalmology approved this retrospective study (IRB 00008855), and informed consent was obtained from all subjects. The described research adhered to the tenets of the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs
Juliette Knoeri http://orcid.org/0000-0002-9229-6296
Vincent Michel Borderie http://orcid.org/0000-0002-1395-8483

REFERENCES

1 Ung L, Bispo PJM, Shanbhag SS, *et al*. The persistent dilemma of microbial keratitis: global burden, diagnosis, and antimicrobial resistance. *Surv Ophthalmol* 2019;64:255–71.
2 Cariello AJ, Passos RM, Yu MCZ, *et al*. Microbial keratitis at a referral center in Brazil. *Int Ophthalmol* 2011;31:197–204.
3 Tam ALC, Côté E, Saldanha M, *et al*. Bacterial keratitis in Toronto: a 16-year review of the microorganisms isolated and the resistance patterns observed. *Cornea* 2017;36:1528–34.
4 Ting DSJ, Ho CS, Cairns J, *et al*. 12-year analysis of incidence, microbiological profiles and in vitro antimicrobial susceptibility of infectious keratitis: the Nottingham infectious keratitis study. *Br J Ophthalmol* 2021;105:328–33.
5 Green M, Carnt N, Apel A, *et al*. Queensland microbial keratitis database: 2005–2015. *Br J Ophthalmol* 2019;103:1481–6.
6 Lin L, Duan F, Yang Y, *et al*. Nine-year analysis of isolated pathogens and antibiotic susceptibilities of microbial keratitis from a large referral eye center in Southern China. *Infect Drug Resist* 2019;12:1295–302.
7 Lin CC, Lalitha P, Srinivasan M, *et al*. Seasonal trends of microbial keratitis in South India. *Cornea* 2012;31:1123–7.
8 Dart JKG, Stapleton F, Minassian D, *et al*. Contact lenses and other risk factors in microbial keratitis. *Lancet* 1991;338:650–3.
9 Hsiao C-H, Sun C-C, Yeh L-K, *et al*. Shifting trends in bacterial Keratitis in Taiwan: a 10-year review in a tertiary-care hospital. *Cornea* 2016;35:313–7.
10 Lorente Pascua J, García Bernal A, Garcia Sanchez E, *et al*. Microorganisms and antibiotic resistance of bacterial keratitis at a rural county hospital in Seville. *Eye & Contact Lens* 2022;48:267–71.
11 Allan BD, Dart JK. Strategies for the management of microbial keratitis. *Br J Ophthalmol* 1995;79:777–86.
12 Ting DSJ, Ho CS, Deshmukh R, *et al*. Infectious keratitis: an update on epidemiology, causative microorganisms, risk factors, and antimicrobial resistance. *Eye* 2021;35:1084–101.
13 Asbell PA, Sanfilippo CM, Sahm DF, *et al*. Trends in antibiotic resistance among ocular microorganisms in the United States from 2009 to 2018. *JAMA Ophthalmol* 2020;138:439–50.
14 Lalitha P, Manoharan G, Karpagam R, *et al*. Trends in antibiotic resistance in bacterial keratitis isolates from South India. *Br J Ophthalmol* 2017;101:108–13.
15 Bourcier T, Thomas F, Borderie V, *et al*. Bacterial Keratitis: predisposing factors, clinical and microbiological review of 300 cases. *Br J Ophthalmol* 2003;87:834–8.
16 Wespiser S, Koestel E, Fabacher T, *et al*. Practice patterns in the management of bacterial keratitis: a five-continent survey. *Graefes Arch Clin Exp Ophthalmol* 2023;261:1961–9.
17 Tan SZ, Walkden A, Au L, *et al*. Twelve-year analysis of microbial keratitis trends at a UK tertiary hospital. *Eye (Lond)* 2017;31:1229–36.
18 Ting DSJ, Settle C, Morgan SJ, *et al*. A 10-year analysis of microbiological profiles of microbial keratitis: the North East England study. *Eye (Lond)* 2018;32:1416–7.
19 Zafar H, Tan SZ, Walkden A, *et al*. Clinical characteristics and outcomes of moraxella keratitis. *Cornea* 2018;37:1551–4.
20 Hoarau G, Merabet L, Brignole-Baudouin F, *et al*. Moraxella keratitis: epidemiology and outcomes. *Eur J Clin Microbiol Infect Dis* 2020;39:2317–25.
21 Tabatabaei SA, Soleimani M, Behrouz MJ, *et al*. A randomized clinical trial to evaluate the usefulness of amniotic membrane transplantation in bacterial keratitis healing. *Ocul Surf* 2017;15:218–26.
22 Liesegang TJ. Contact lens-related microbial keratitis: part I: epidemiology. *Cornea* 1997;16:125–31.
23 Basak SK, Basak S, Mohanta A, *et al*. Epidemiological and microbiological diagnosis of suppurative keratitis in Gangetic West Bengal, Eastern India. *Indian J Ophthalmol* 2005;53:17–22.
24 Ung L, Chodosh J. Foundational concepts in the biology of bacterial keratitis. *Exp Eye Res* 2021;209:108647.
25 Khoo P, Cabrera-Aguas MP, Nguyen V, *et al*. Microbial keratitis in Sydney, Australia: risk factors, patient outcomes, and seasonal variation. *Graefes Arch Clin Exp Ophthalmol* 2020;258:1745–55.
26 Lim NCS, Lim DKA, Ray M. Polymicrobial versus monomicrobial keratitis: a retrospective comparative study. *Eye Contact Lens Sci Clin Pract* 2013;39:348–54.
27 Jones DB. Polymicrobial keratitis. *Trans Am Ophthalmol Soc* 1981;79:153–67.
28 Almulhim A, Alkhalifah MI, Kalantan H, *et al*. Bacterial keratitis: clinical features, causative organisms, and outcome during a 13-year study period. *Cornea* 2023;42:702–7.
29 Pakzad-Vaezi K, Levasseur SD, Schendel S, *et al*. The corneal ulcer one-touch study: a simplified microbiological specimen collection method. *Am J Ophthalmol* 2015;159:37–43.
30 Kaye SB, Rao PG, Smith G, *et al*. Simplifying collection of corneal specimens in cases of suspected bacterial keratitis. *J Clin Microbiol* 2003;41:3192–7.
31 Ibrahim YW, Boase DL, Cree IA. Epidemiological characteristics, predisposing factors and microbiological profiles of infectious corneal ulcers: the Portsmouth corneal ulcer study. *Br J Ophthalmol* 2009;93:1319–24.
32 Ting DSJ, Cairns J, Gopal BP, *et al*. Risk factors, clinical outcomes, and prognostic factors of bacterial keratitis: the Nottingham infectious keratitis study. *Front Med (Lausanne)* 2021;8:715118.
33 Miedziak AI, Miller MR, Rapuano CJ, *et al*. Risk factors in microbial keratitis leading to penetrating keratoplasty. *Ophthalmology* 1999;106:1166–70.
34 Ray KJ, Prajna L, Srinivasan M, *et al*. Fluoroquinolone treatment and susceptibility of isolates from bacterial keratitis. *JAMA Ophthalmol* 2013;131:310–3.
35 Chang VS, Dhaliwal DK, Raju L, *et al*. Antibiotic resistance in the treatment of Staphylococcus aureus keratitis: a 20-year review. *Cornea* 2015;34:698–703.
36 Termote K, Joe AW, Butler AL, *et al*. Epidemiology of bacterial corneal ulcers at tertiary centres in Vancouver, B.C. *Can J Ophthalmol* 2018;53:330–6.
37 Shah VM, Tandon R, Satpathy G, *et al*. Randomized clinical study for comparative evaluation of fourth-generation fluoroquinolones with the combination of fortified antibiotics in the treatment of bacterial corneal ulcers. *Cornea* 2010;29:751–7.
38 Chatterjee S, Agrawal D, Gomase SN, *et al*. Fluoroquinolone resistance in bacterial isolates from ocular infections: trend in antibiotic susceptibility patterns between 2005-2020. *Indian J Ophthalmol* 2022;70:4391–8.

Br J Ophthalmol: first published as 10.1136/bjo-2024-325261 on 26 June 2024. Downloaded from http://bjo.bmj.com/ on August 10, 2024 by guest. Protected by copyright.